Standardized evaluation of Tumor-Infiltating Lymphocytes (TIL) in Breast Cancer for daily clinical and research practice or clinical trial setting

A tutorial prepared by the International Working Group for TIL in breast cancer – 2014 – adapted 2020

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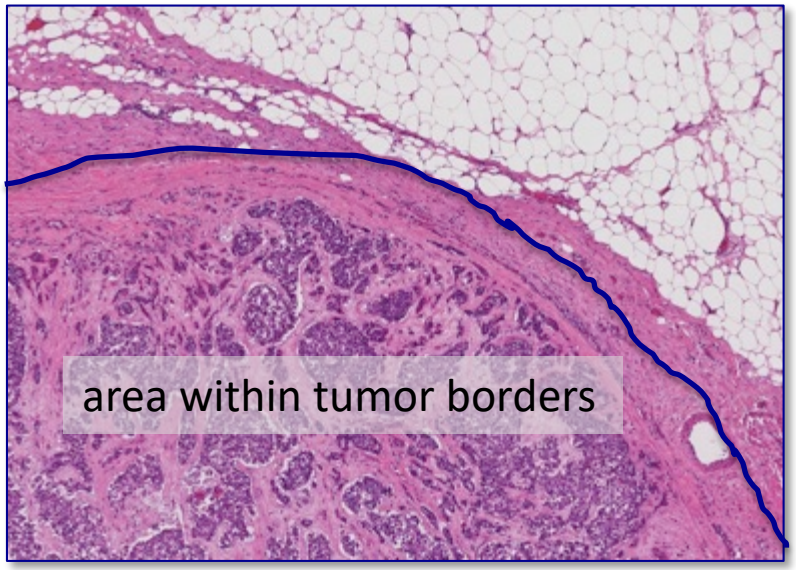
Aim of this tutorial

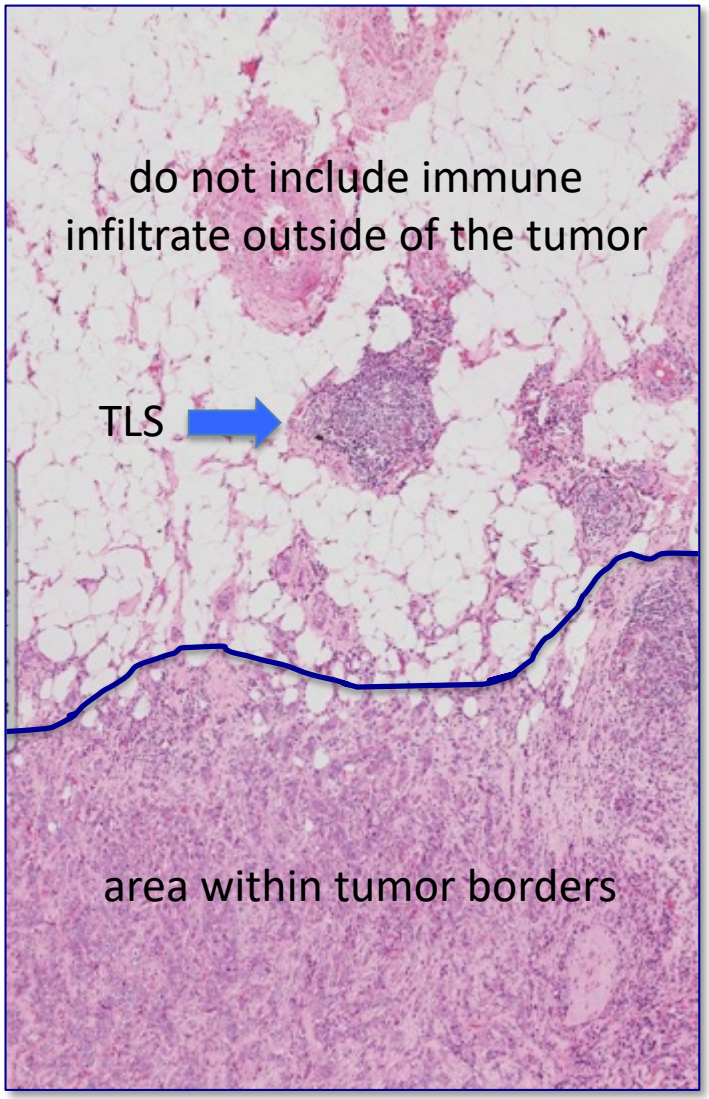
- To provide a guideline to pathologists for the standardized evaluation of tumor-infiltrating lymphocytes based on H&E slides of core biopsies or tumor resections.
- Please consult the manuscript for more specific details.

Step 1: Define area for TIL evaluation

- Only TILs within the borders of the invasive tumors are evaluated
- The invasive edge is included in the evaluation, but not reported separately
- Immune infiltrates outside of the tumor borders, e.g. in adjacent normal tissue or DCIS are not included



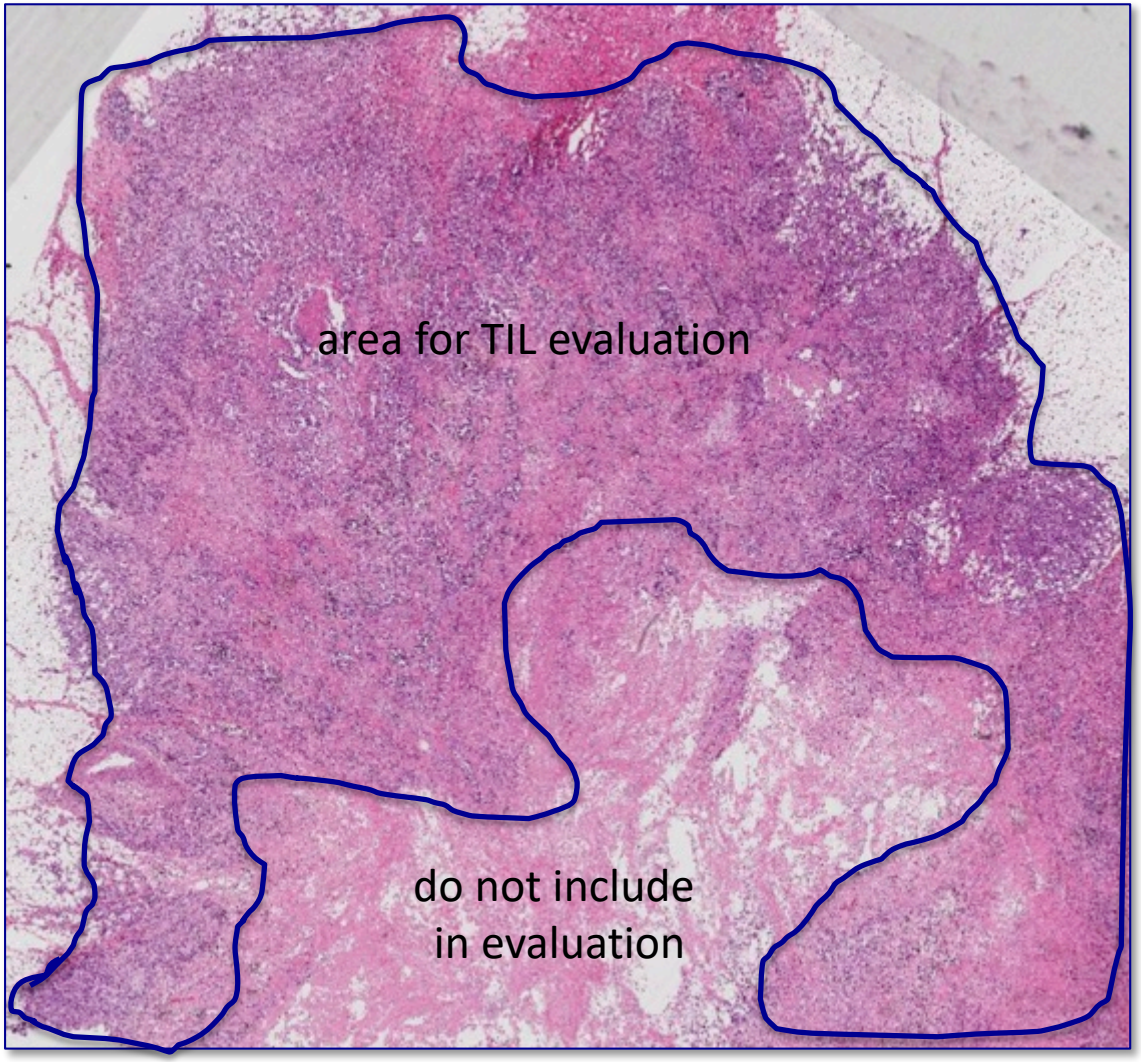
Example 1



Example 2

Step 1: Define area for TIL evaluation

- Large areas of central necrosis or fibrosis are not included in the evaluation

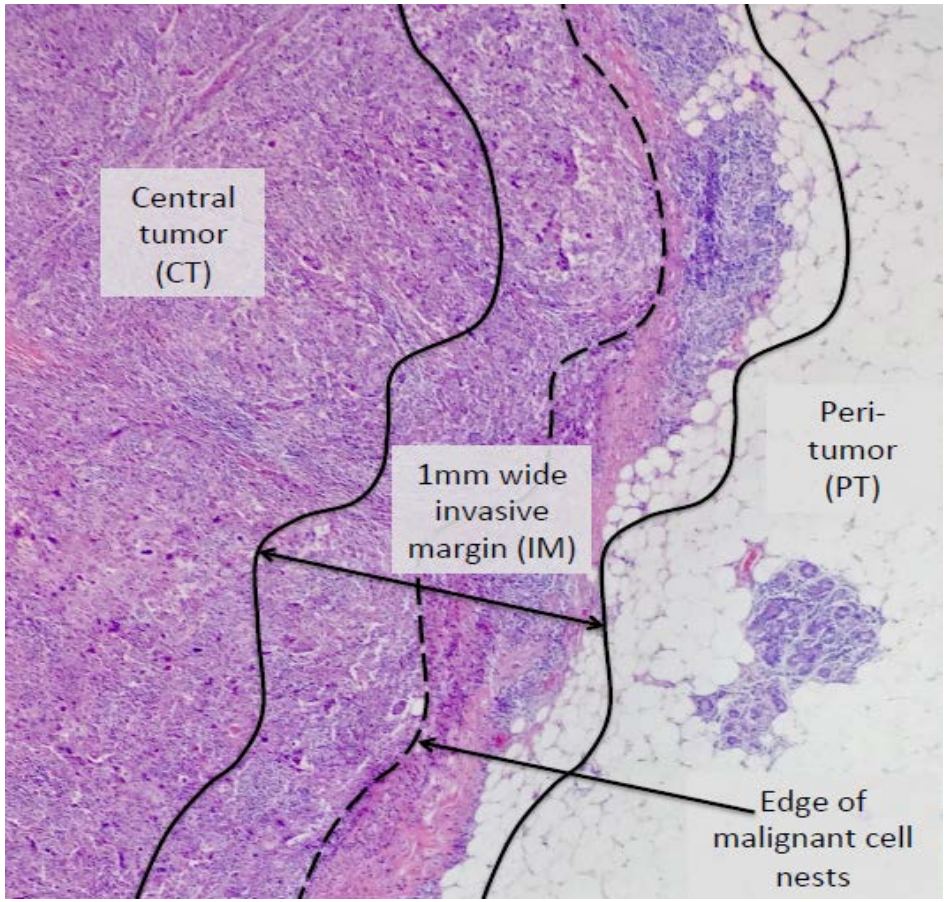


Example 3

Step 1: Define the invasive margin

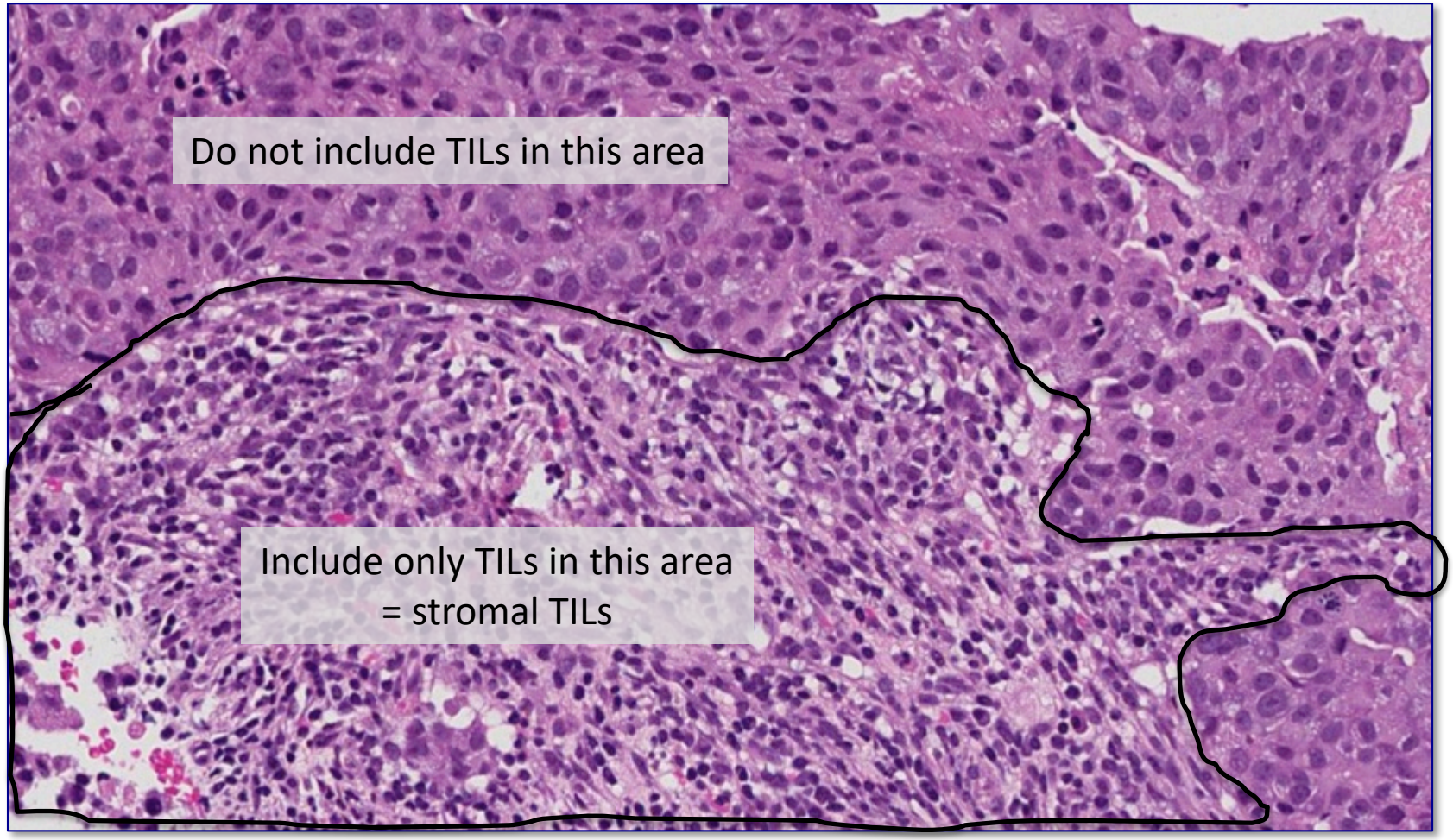
Shona Hendry et al. 2017

- The "invasive margin" is defined as a 1 mm region centered on the border separating the malignant cell nests from the host tissue.
- The "central tumor" represents the remaining tumor area.



Step 2: Focus on stromal TIL

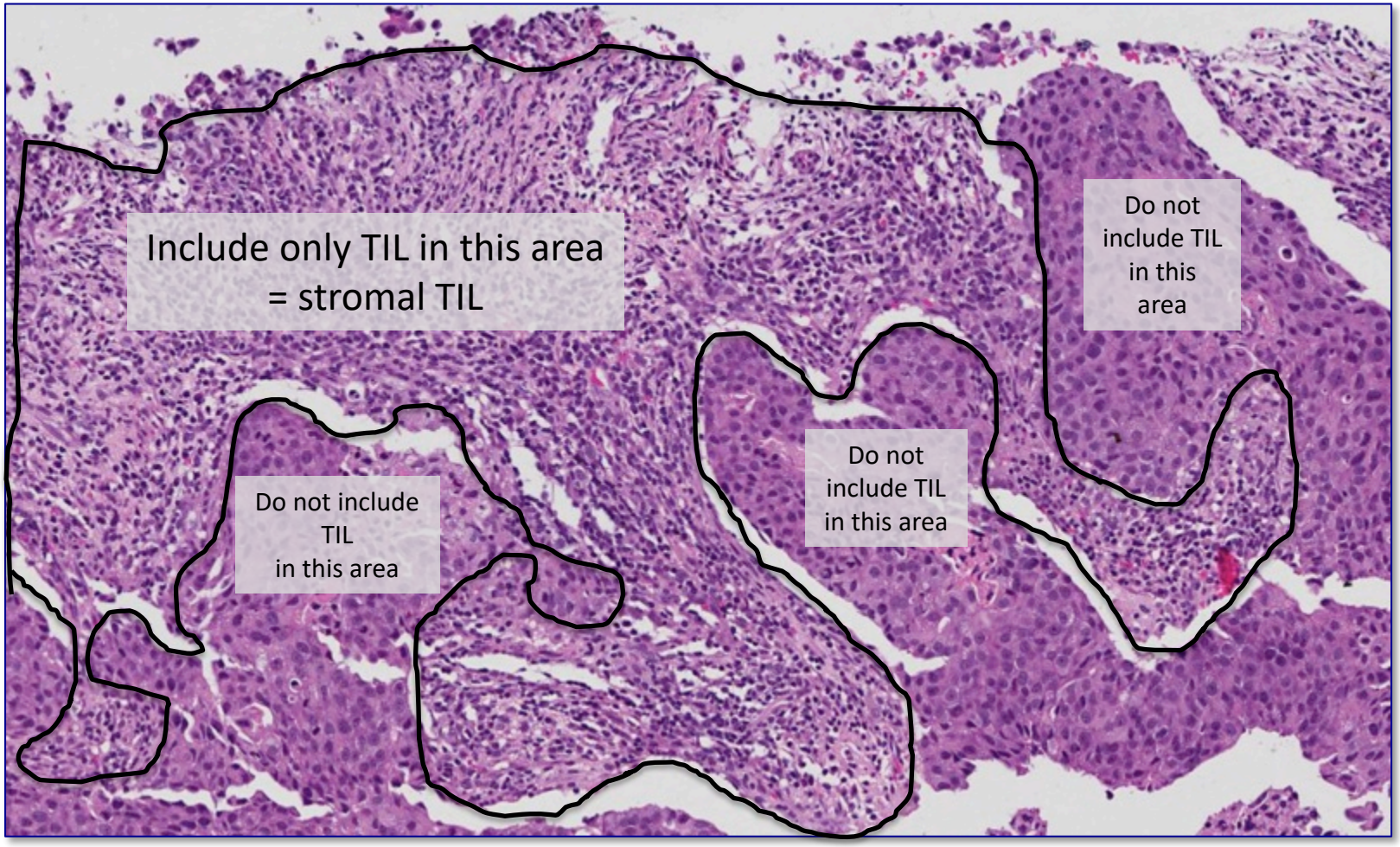
- In the diagnostic setting, only stromal TILs are relevant



Example 4

Step 2: Focus on stromal TIL

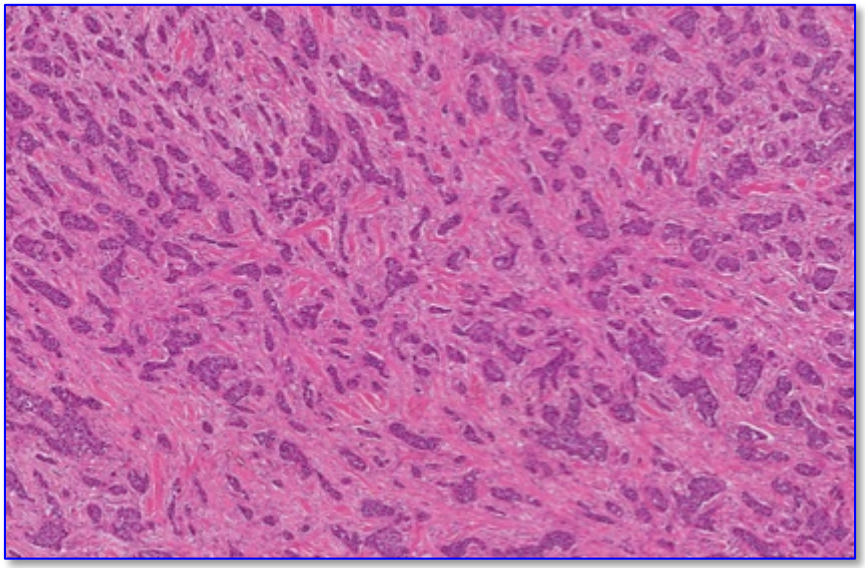
- in the diagnostic setting, only stromal TIL are relevant



Example 5

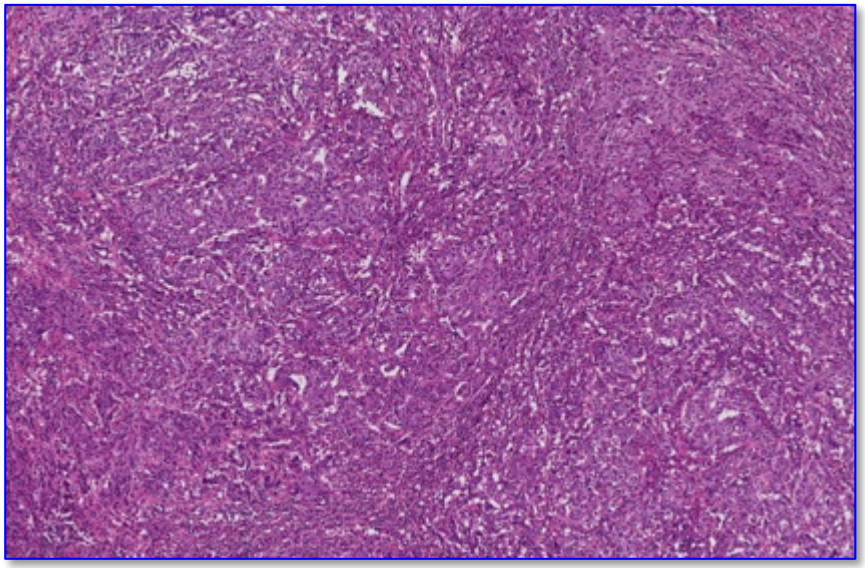
Step 2: Scan tumor at low magnification – focus on the tumor stroma

- Stroma contains predominantly collagenous tissue, few round cells



Example 6

- Stroma contains predominantly round cell infiltrate, collagenous tissue difficult to recognize



Example 6

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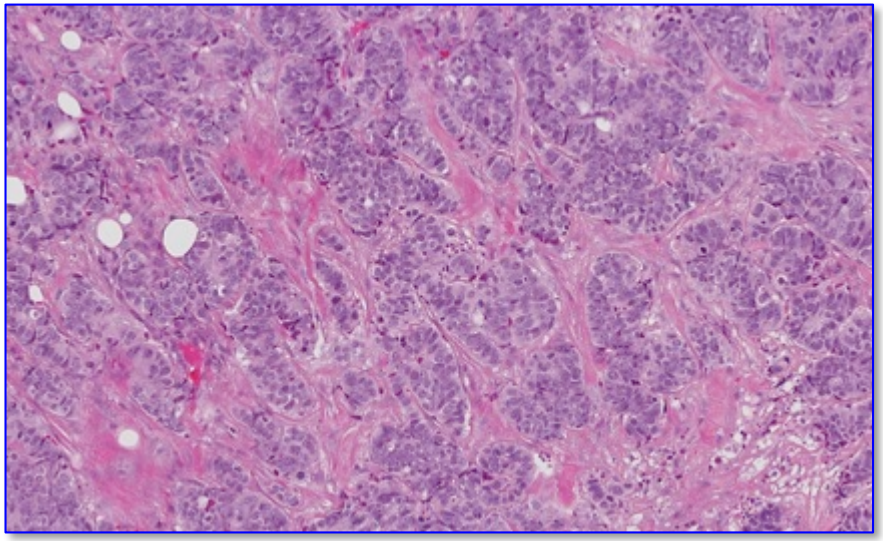
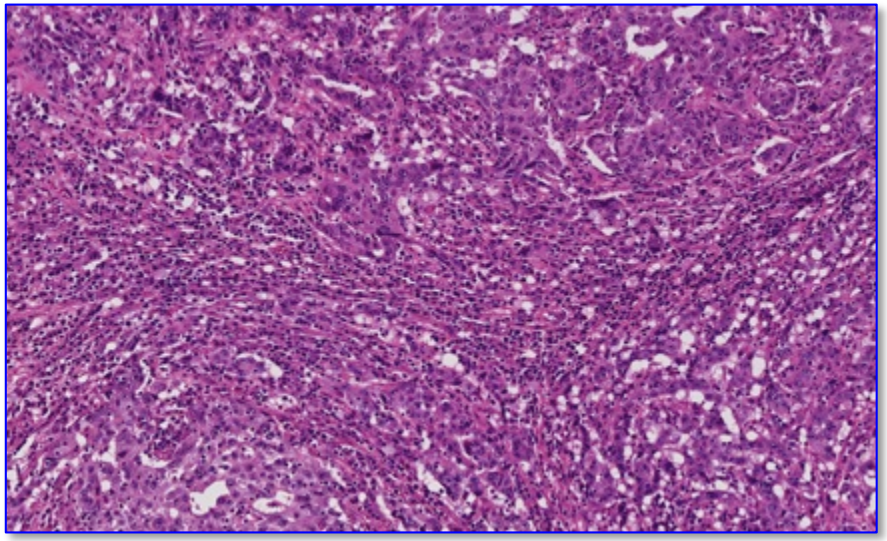
- Stroma contains predominantly collagenous tissue, few round cells



Example 8

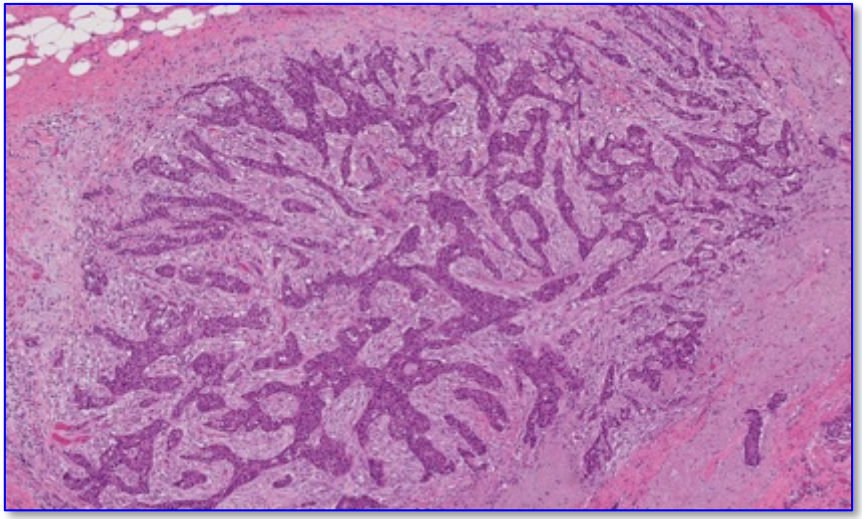
- Stroma contains predominantly round cell infiltrate, collagenous tissue difficult to recognize



Example 9

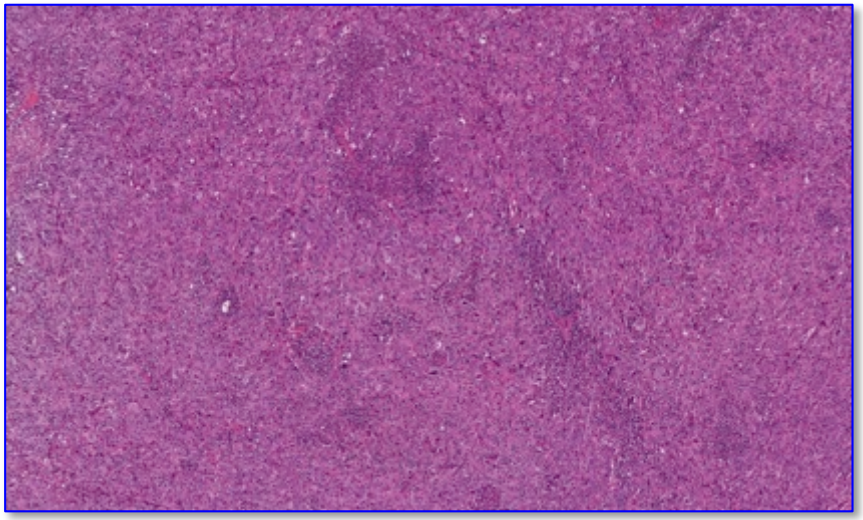
Step 2: Scan tumor at low magnification – focus on the tumor stroma

- Stroma contains predominantly collagenous tissue, few round cells



Example 10

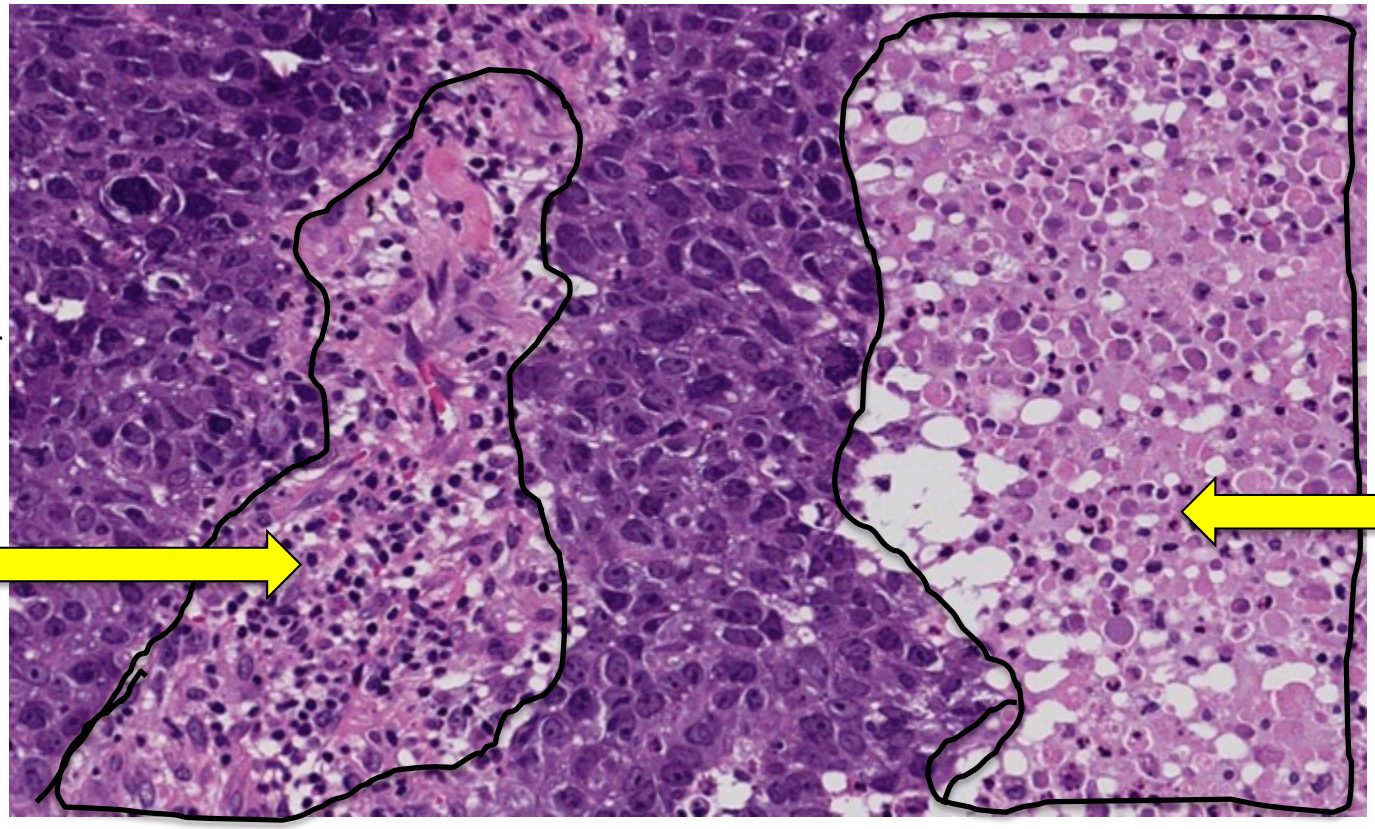
- Stroma contains predominantly round cell infiltrate, collagenous tissue difficult to recognize



Example 11

Step 3: Determine type of inflammatory infiltrate

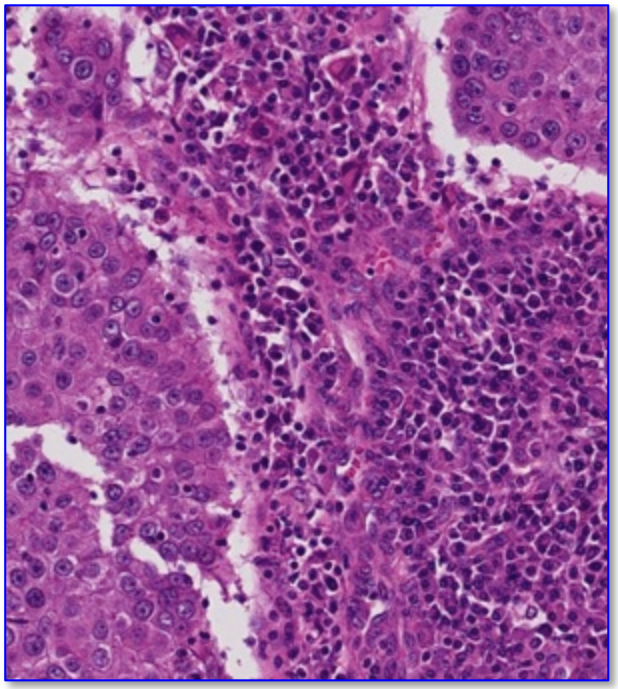
- Include only mononuclear infiltrate (lymphocytes & plasma cells)
- Do not include granulocytic infiltrate in areas of tumor necrosis



Example 12

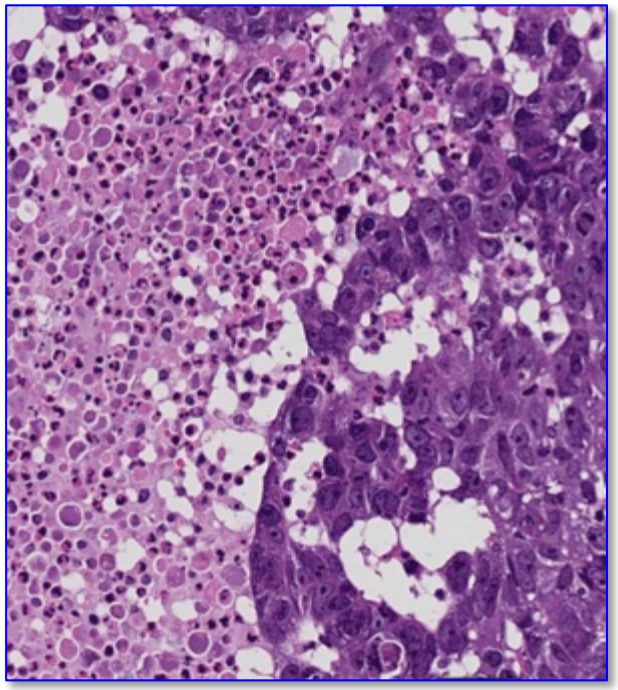
Step 3: Determine type of inflammatory infiltrate

- Include only mononuclear infiltrate (lymphocytes & plasma cells)



Example 13

- do not include granulocytic infiltrate in areas of tumor necrosis



Example 14

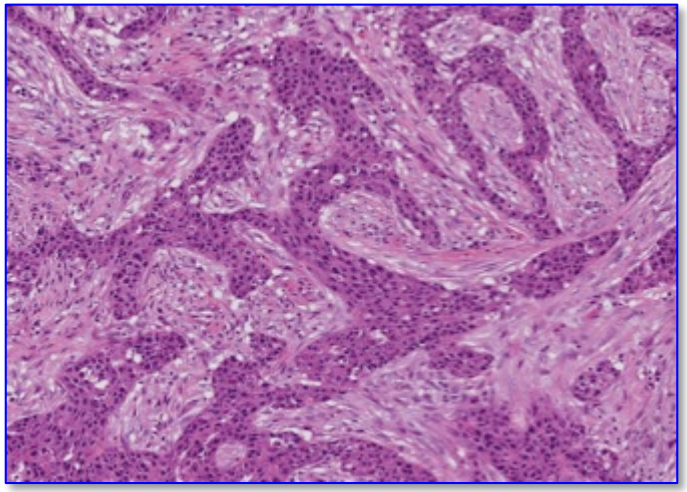
Step 4: As a first approach, include tumor in one of three groups based on low magnification and assess % stromal TILs (continue with Step 5 for percentage)

Group A: tumor with no/minimal immune cells

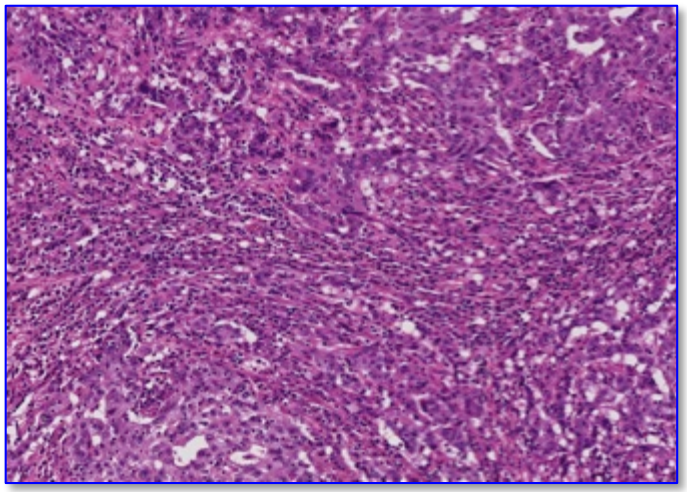
Group B: tumor with intermediate / heterogeneous infiltrate

Group C: tumor with high immune infiltrate

0-10% stromal TILs | 10-40% stromal TILs | 40-90% stromal TILs



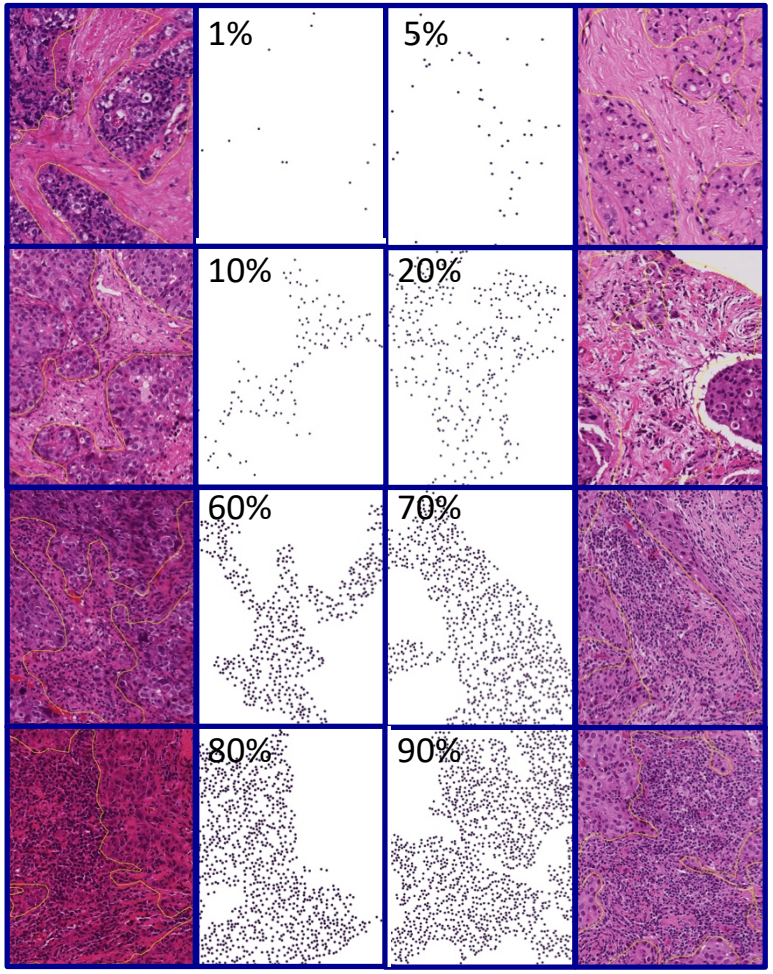
For this intermediate group evaluate different areas at higher magnification.



Example 15

Example 16

Step 5: Report percentage of stromal lymphocytes



- Report the average of the stromal area, do not focus on hot spots.
- For intermediate group evaluate different areas at higher magnification.
- Please note that lymphocytes to not form solid aggregates, therefore even with 90-100% stromal TILs there will still be some space between the individual lymphocytes.

Please send any questions or comments to:

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